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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,519	03/03/2000	JAMES B. MITCHELL	175931	8084

45733 7590 11/28/2005

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,519	MITCHELL ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,9-20,28,30-34,36-47 and 49* is/are pending in the application.

4a) Of the above claim(s) *4-7,9-20,31-34 and 36-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,28, 30 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114. Claims 1, 28, 30 and 49 are currently pending for prosecution on the merits.

Response to Arguments

2. Applicant's arguments with respect to claims 1, 28, 30 and 49 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 28, 30 and 49 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to the instantly claimed "prodrug thereof" (claims 1, 28, 30 and 49),

The claims are directed to a method for slowing the progression of a tumor or delaying the onset of tumor formation by administering compound of Formula I or prodrug thereof,

wherein said tumor is due to genetic defect in the p53 gene (claims 1, 30 and 49) or said tumor is due to ataxia telangiectasia or Li Fraumeni syndrome (claim 28).

The specification discloses that the nitroxide or prodrug thereof to be administered is preferably alicyclic or heterocyclic compound of Formula I or Formula II. Particularly, the specification discloses the results of study involving Tempol, or sugar-water treated p53 knock-out mice (KO1), wherein the study shows that both Tempol-treated mice and sugar-water-treated mice group ultimately develop cancers, but the percent survival is increased in Tempol-treated group (page 16, lines 4-6). Declaration, filed 9/22/03, shows that Tempol is useful in prolonging the lifespan of p53 deficient mice.

As discussed above, the specification discloses a method for slowing the progression of a tumor by administering Tempol (broadly compounds of Formula I), which meets the written description. However, claim 1 is directed to encompass any prodrugs, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. None of these meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of Compounds of Formula I, the skilled artisan cannot envision how to make/use "prodrug thereof". Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

With respect to "tumor due to ataxia telangiectasia or Li Fraumeni syndrome" (claim 28),

The claim is directed to a method for slowing the progression of a tumor or delaying the onset of tumor formation by administering compound of Formula I or prodrug thereof to an

animal at risk for developing tumor or having tumor due to ataxia telangiectasia or Li graumeni syndrome.

The specification discloses the results of study involving a compound of Formula I, namely Tempol, or sugar-water treated p53 knock-out mice (KO1), wherein the study shows that both Tempol-treated mice and sugar-water-treated mice group ultimately develop cancers, but the percent survival is increased in Tempol-treated group (page 16, lines 4-6). Declaration, filed 9/22/03, shows that Tempol is useful in prolonging the lifespan of p53 deficient mice.

Although the instant specification discloses the efficacy of a nitroxide, namely Tempol, in slowing the progression of tumor related to p53 tumor suppressor gene mutation (Examples 1-2), none of the Examples do not clearly point out which types of cancers are responsive to the administration of nitroxide or which types of cancers originate from a defect of the p53 gene. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds for tumor due to ataxia telangiectasia or Li Fraumeni syndrome.

With the exception of skin cancer or probable spleen cancer, the skill artisan cannot envision how to treat Ataxia Telangiectasia or Li Fraumeni syndrome. As discussed above, there is no correlation on this record between in p53 -/- mice study and a practical utility in ataxia telangiectasia or Li Fraumeni syndrome. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of the treatment.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1, 28, 30 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims refer to the suitable compounds for the instant invention as "compound of Formula I or prodrug thereof". Looking at the prosecution history (prior the entry of the amendment filed August 03, 2005), the applicant has been referred to the suitable compounds for the claimed invention as "said nitroxide or prodrug thereof is a compound of Formula I... " (see page 7, lines 25-26 of the disclosure and the claims filed September 22, 2003). In other words, "said prodrug" was only limited to the compound of Formula I. However, the instantly claimed prodrug broadens the scope of the invention. Apparently, this inconsistency leads to lack of clarity of the claims as a whole.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claim 1, 30 and 49 are rejected under 35 U.S.C. 102(e) as being anticipated by Bernstein (US 5840734).

Bernstein teaches the administration of Tempol to individuals undergoing photodynamic therapy for skin cancer or psoralen treatment for cancer to protect humans from developing skin cancer (column 5, lines 43-56 and claims1-4).

Although Bernstein is silent regarding the characteristic of said Tempol in "slowing the progression of a tumor" or "delaying the onset of tumor formation", the prior method of administration the same compound inherently possessing a therapeutic effect for the same ultimate purpose as disclosed by Applicants anticipates Applicant's claims even absent explicit recitations of the mechanism.

Since the referenced skin cancer "metes and bounds" applicant's broadly defined "tumor due to a genetic defect in the p53 gene", the reference anticipates the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 28 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 of U.S. Patent No. US 5,462,946 or claim 2 of US 6,605,619. Although the conflicting claims are not identical, they are not patentably distinct from each other because the prior methods of administering the same 4-hydroxy-2,2,6,6,-tetramethylpiperidine-1-oxyl (Tempol) to the animals inherently possessing a therapeutic effect for the same ultimate purpose as disclosed by Applicants anticipates Applicant's claims even absent explicit recitations of the mechanism.

Since the referenced effective dosage amounts (See page 15, lines 56-66 of US'619 and claim 22 of US'946) overlap with the claimed dosage amount in 'delaying the onset of tumor formation" (about 0.1 to about 100mg/kg/body weight, See page 11, lines 5-11 of the instant specification), as discussed above, the referenced method of administering the same compound in overlapping dosage amount to the same treatment group (i.e., any animal or any animal at risk for developing a tumor) make obvious the claimed invention.

Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614